Article

Clofazimine: another potential magic bullet for the treatment of COVID-19?

Egiz, Abdullah Mohammed abousaleh ma and Gala, Dhir Niren

Egiz, Abdullah Mohammed abousaleh ma orcid iconORCID: 0000-0003-0304-7982 and Gala, Dhir Niren orcid iconORCID: 0000-0003-1410-8576 (2021) Clofazimine: another potential magic bullet for the treatment of COVID-19? Postgraduate Medical Journal . ISSN 0032-5473

It is advisable to refer to the publisher's version if you intend to cite from the work.
http://dx.doi.org/10.1136/postgradmedj-2021-140143

Clofazimine: Another Potential Magic Bullet for The Treatment of COVID-19?

Authors: Abdullah Egiz, Dhir N. Gala.

Affiliations: School of Medicine, University of Central Lancashire, Preston, UK

To the Editor,

As of March 2020, the novel coronavirus disease 2019 (COVID-19) caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) was declared a pandemic. The novelty of the virus is the driving force for numerous clinical trials taking place in an attempt to discover appropriate therapeutic agents.[1] Many pharmacological agents have shown promising results, including Clofazimine.[2,3] More recently, a prospective open-label randomised controlled clinical trial of dual therapy with interferon beta-1b and Clofazimine for COVID-19 patients is being conducted.

Clofazimine is licensed for use against mycobacterial infection and as an adjunct agent for the treatment of multibacillary leprosy. However, it has also proven to comprise immunosuppressive properties.[2] Therefore, we would like to outline a potential use for Clofazimine in COVID-19 infections, where it could be a potential prophylactic and therapeutic agent in the management of critically ill patients.

The most important cause of mortality post-infection with COVID-19 is a cytokine storm leading to end organ damage from inflammation.[2] Thus, one of the main therapeutic treatments being used

to increase survival, reduce inflammatory sequelae and decrease hospitalization following COVID-19 pneumonia are anti-inflammatory drugs. Clofazimine is an antibiotic with anti-inflammatory properties, which can potentially be used for the treatment of COVID-19.[2,3]

In patients with severe infection leading to cytokine storm, the use of immunosuppressive agents has proven beneficial.[2,3] Indeed, clofazimine can inhibit the proliferation and activation of T-lymphocytes through inhibition of the sodium-potassium ATPase.[3,4] This immunomodulatory effect of clofazimine has proven beneficial in the treatment of autoimmune disorders such as psoriasis and multiple sclerosis.[4] Yuan et al., (2020) reported significant decrease in the mRNA expression of IL-6 ($p=0.0001$), TNF-α ($p=0.0006$), and CCR4 ($p=0.0029$) in the hamsters treated with clofazimine.[2]

Interestingly, antiviral synergistic effects have been reported when Clofazimine is co-administered with Remdesivir.[2] The co-application of clofazimine and remdesivir in an in-vitro cellular assay with a 10% concentration of fetal bovine serum resulted in a nearly 20-fold reduction in the concentrations of remdesivir required to inhibit viral replication by 90%. This synergistic pharmacological effect did not elicit detectable cytotoxic changes. However, to further narrow the in-vivo side effects profile, clofazimine can be administered via inhalation reducing its systemic side effects such as skin discoloration and gastrointestinal discomfort.[5]

In summary, clofazimine with its anti-inflammatory and immunomodulatory effect with minimal side-effects could increase survival in critically ill patients infected with the COVID-19 virus.

Contributors

AE and DNG designed and cowrote the manuscript. Both AE and DNG did the data collection, data analysis and interpretation. Both AE and DNG designed the conceptualization and contributed to the manuscript.

Funding

The authors have not declared a specific grant for this research from any funding agency in the public, commercial or not-for-profit sectors.

Competing interests

None declared.

Patient consent for publication

Not required.

Provenance and peer review

Not commissioned, internally peer reviewed.

References

1 Wong C, Wan E, Luo S, Ding Y, Lau E, Ling P et al. Clinical outcomes of different therapeutic options for COVID-19 in two Chinese case cohorts: A propensity-score analysis. EClinicalMedicine. 2021;32:100743.

2 Yuan S, Yin X, Meng X, Chan J, Ye ZW, Riva L, et al. Clofazimine is a broad-spectrum coronavirus inhibitor that antagonizes SARS-CoV-2 replication in primary human cell culture and hamsters. Research square. 2020; doi:10.21203/rs.3.rs-86169/v1

3 Wan W, Zhu S, LiS, Shang W, Zhang R,LiH,et al. High-Throughput Screening of an FDA-Approved Drug Library Identifies Inhibitors against Arenaviruses and SARS-CoV-2. ACS infectious diseases. 2020; doi:10.1021/acsinfecdis.0c00486

4 Cholo MC, Steel HC, Fourie PB, Germishuizen WA, Anderson R. Clofazimine: current status and future prospects. Journal of antimicrobial chemotherapy. 2012;67(2):290-8.

5 Banaschewski B, Verma D, Pennings LJ, Zimmerman M, Ye Q, Gadawa J, et al.Clofazimine inhalation suspension for the aerosol treatment of pulmonary nontuberculous mycobacterial infections. Journal of Cystic Fibrosis. 2019;18(5):714-20.